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Publication date:
2019

Document Version
Publisher's PDF, also known as Version of record

P285

Intra-articular gold micro particles relieve pain in knee osteoarthritis -A pilot study

Sten Rasmussen [1, 2, 3,] Kristian Kjær Petersen[1], Lars Arendt-Nielsen[1]

[1)]Center for Sensory-Motor Interaction (SMI), CNAP, School of Medicine, Aalborg University, Aalborg Denmark
[2)]Department of Clinical Medicine, School of Medicine, Aalborg University, Aalborg Denmark
[3)]Department of Orthopedic Surgery, Aalborg University Hospital, Aalborg, Denmark

Background and aims

Many patients suffering from osteoarthritis (OA) do not get adequate pain relieve. Evidence suggest an inflammatory component in OA pain.

The immuno-modulatory effect of gold ions have for more than 50 years a known anti-inflammatory effect in the treatment of rheumatic arthritis. Gold ions alter the function of macrophages by inhibiting lysosomal enzymes and lowering production of pro-inflammatory cytokines (1-2).

Dissolucytotic metallic gold (DMG) ions have an immune-suppressive effect in laboratory testing (3-6) (Figure 1 - 4). Animal studies prove the effect of gold implantation in arthritic joints (7-10). Injection of DMG in animal models stimulate the immune system (11-12). The carrier for injecting the DMG micro particles is hyaluronic acid (13-14).

No studies have investigated the effect of intraarticular gold micro particle implants for treatment of knee osteoarthritis in humans. The present open pilot study aimed to investigate if gold ions released from intra-articular gold micro particles have a role in treating knee OA (15).

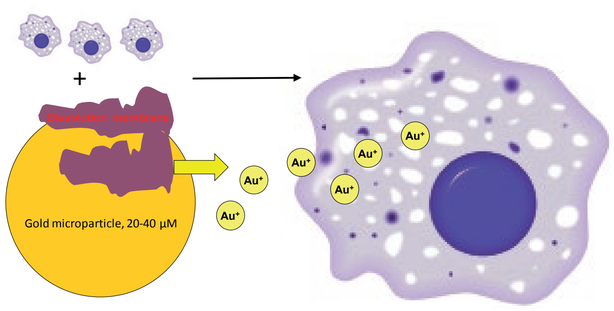

Figure 1. Macrophages controls the dissolution membrane which liberate the gold ions by oxidation of the surface. Once the ions are liberated, most likely as Au(CN) , they are free to diffuse through the immediate microenvironment. The gold-loaded molecules are taken up into the cells, primarily macrophages, mastcells and histocytes.

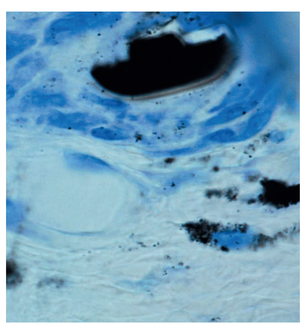

Figure 2. Close to the gold implant gold-loaded molecular clusters are located outside cells. The two loaded cells are believed to be macrophages loaded with gold ions. The gold ions accumulate primarily in the lysosymes (3).

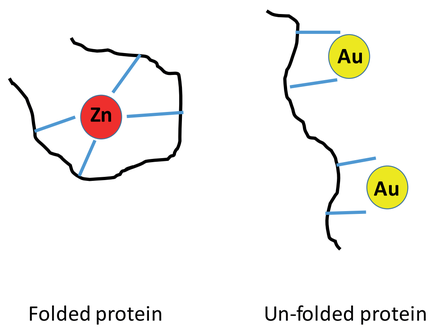

Figure 3. Once in the intercellular fluid and the intracellular compartments, the gold ions act in the same ways that have been demonstrated for systemically administered gold ions. The effect is related to the ability of the gold ions to unfold the protein structures.

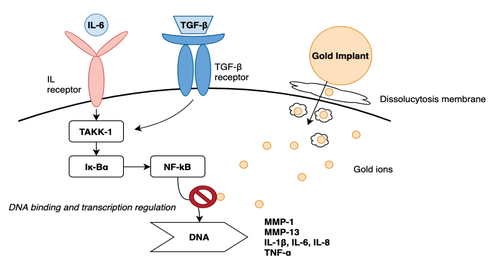

Figure 4. Gold ions suppress inflammation locally by affecting certain signalling molecules and binding enzymes essential for the inflammatory process. The DNA binding activity and transcription regulation of NF-kB is abolished when AU- ions replace Zn2+ ions. (4)

Methods

A cohort of 30 patients, aged ≥18years, pain ≥ 3 months, synovial effusion on MRI, and Kellgren-Lawrence OA grade 3-4 were included. Metallic gold 20 mg, 72.000 pieces, 20-40 µ-meter (Berlock-Micro-Implants, HumanGoldInject) (13-14) were injected into the knee joint using the patient's own synovial fluid as the carrier. The primary outcome measure was temporal summation of pain (TSP). The secondary outcome measures were Conditioned Pain Modulation (CPM), knee Pressure Pain Threshold (PPT), the PainDetect score, and the Western Ontario and McMaster Universities Arthritis Index (WOMAC).

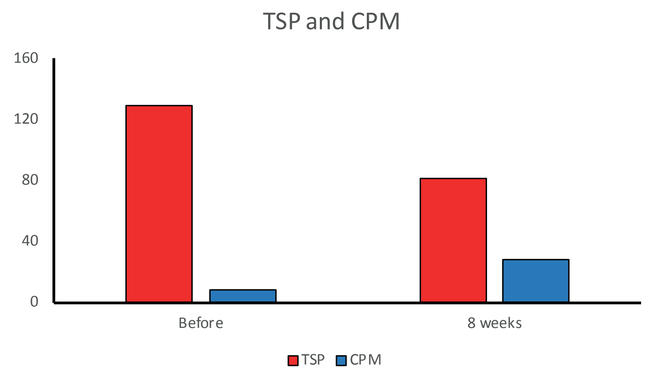

Figure 5

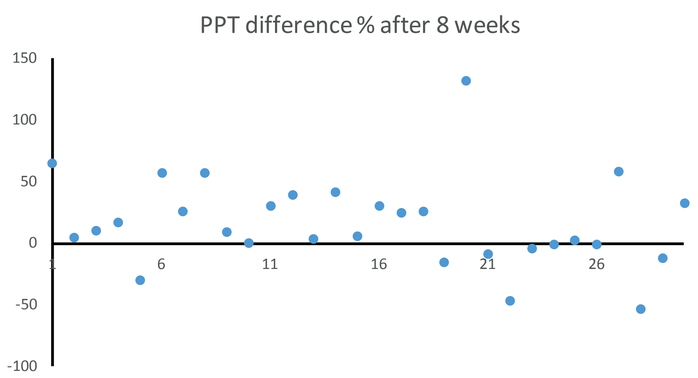

Figure 6

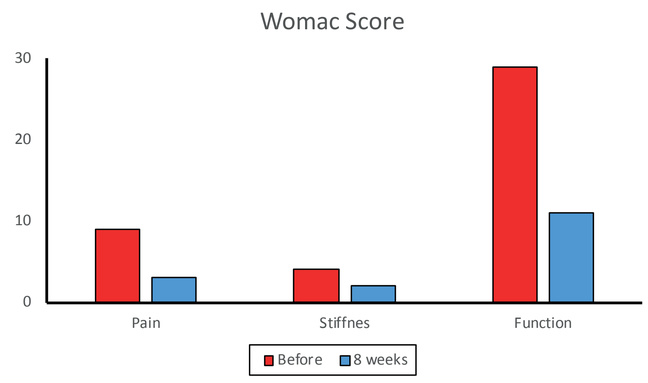

Figure 7

Results

TSP was reduced 37.5 % (P = 0.027) and CPM was improved 22.4 % (P = 0.026) (Figure 5). PPT increased 10 % (P = 0.0001) (figure 6). PainDetect was reduced from 10 (1-26) to 3 (0-19) (P = 0.0005), WOMAC pain decreased from 9 (6-16) to 3 (0-15) (P = 0.0001), stiffness from 4 (1-8) to 2 (0-8) (P = 0.036) and function improved from 29 (14-51) to 11 (0-41) (P = 0.0009) (figure 7).

Conclusions

The significant improvements in pain caused by the intraarticular gold micro particles indicate an inhibition of inflammation. The significant improvements in qualitative sensory tests indicate less pain hyperalgesia.

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